



Dolan, R. D., Daly, L., Sim, W. M.J., Fallon, M., Ryan, A., McMillan, D. C. and Laird, B. J. (2020) Comparison of the prognostic value of ECOG-PS, mGPS and BMI/WL: implications for a clinically important framework in the assessment and treatment of advanced cancer. *Clinical Nutrition*, 39(9), pp. 2889-2895.
(doi: [10.1016/j.clnu.2019.12.024](https://doi.org/10.1016/j.clnu.2019.12.024))

There may be differences between this version and the published version. You are advised to consult the publisher's version if you wish to cite from it.

<http://eprints.gla.ac.uk/208833/>

Deposited on 8 June 2020

Enlighten – Research publications by members of the University of Glasgow
<http://eprints.gla.ac.uk>

Comparison of the prognostic value of ECOG-PS, mGPS and BMI/WL: Implications for a clinically important framework in the assessment and treatment of advanced cancer

Ross D Dolan^{1a}, Louise Daly^{2a}, Wei MJ Sim¹, Marie Fallon³, Aoife Ryan², Donald C McMillan^{1b}, Barry J Laird^{3b}

Affiliation(s):¹Academic Unit of Surgery, School of Medicine, University of Glasgow, Glasgow Royal Infirmary, Glasgow, UK; ²School of Food and Nutritional Sciences, College of Science, Engineering and Food Science, University College Cork, Cork, Ireland; ³Edinburgh Cancer Research Centre, Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh UK.

a: Joint first author b: Joint senior author

Corresponding author:

Ross Dolan, Clinical Research Fellow,
Academic Unit of Surgery, University of Glasgow,
New Lister Building, Glasgow Royal Infirmary,
Glasgow,
G4 0SF,
United Kingdom.

Email: Ross.Dolan@glasgow.ac.uk

Tel: 0141 211 4000 **Fax:** 0141 211 4943

Short Title: Prognostication of ECOG-PS/mGPS & BMI/WL in cancer

Keywords: Advanced cancer, systemic inflammation, Glasgow Prognostic Score, body composition, ECOG, physical function testing, computed tomography.

Conflicts of Interest: The authors declare no potential conflicts of interest

Funding: This study was funded by the University of Glasgow

Abstract:

Background and Aims: The systemic inflammatory response is associated with the loss of lean tissue, anorexia, weakness, fatigue and reduced survival in patients with advanced cancer and therefore is important in the definition of cancer cachexia. The aim of the present study was to carry out a direct comparison of the prognostic value of Eastern Cooperative Oncology Group Performance Status (ECOG-PS), modified Glasgow Prognostic Score (mGPS) and Body Mass Index/Weight Loss Grade (BMI/WL grade) in patients with advanced cancer.

Method: All data were collected prospectively across 18 sites in the UK and Ireland. Patient's age, sex, ECOG-PS, mGPS and BMI/WL grade were recorded, as were details of underlying disease including metastases. Survival data were analysed using univariate and multivariate Cox regression.

Results: A total of 730 patients were assessed. The majority of patients were male (53%), over 65 years of age (56%), had an ECOG-PS>0/1 (56%), mGPS \geq 1 (56%), BMI \geq 25 (51%), <2.5% weight loss (57%) and had metastatic disease (86%). On multivariate cox regression analysis ECOG-PS (HR 1.61 95%CI 1.42-1.83, p<0.001), mGPS (HR 1.53, 95%CI 1.39-1.69, p<0.001) and BMI/WL grade (HR 1.41, 95%CI 1.25-1.60, p<0.001) remained independently associated with overall survival. In patients with a BMI/WL grade 0/1 both ECOG and mGPS remained independently associated with overall survival.

Conclusion: The ECOG/mGPS framework may form the basis of risk stratification of survival in patients with advanced cancer.

50 **Statement of Significance:**

51 This study shows that the ECOG/mGPS framework had prognostic value where BMI/WL
52 was normal. This would suggest that the ECOG/mGPS framework may form the basis of risk
53 stratification of survival and provide diagnostic criteria for cachexia in patients with
54 advanced cancer. Furthermore, it would redirect clinical efforts to treat cachexia.

55

56

Introduction

The recognition of the poor prognosis associated with the syndrome of cachexia dates back to ancient Greece. These observations remain valid today as in patients with advanced cancer, progressive involuntary loss of body weight and lean tissue, anorexia, weakness and fatigue (cancer cachexia) are associated with poor survival[1]. Despite the clinical recognition of the syndrome of cancer cachexia, performance status remains the most routinely assessed clinical measure on which to base likely patient outcome to treatment and prognosis [2].

There is now consistent evidence that the presence of a systemic inflammatory response, as evidenced by the modified Glasgow Prognostic Score (mGPS) is associated with the loss of lean tissue, anorexia, weakness and fatigue and poor survival in patients with advanced cancer [3, 4]. Moreover, the mGPS, in combination with ECOG-PS, has been shown to effectively stratify the above measures of cachexia [2, 5].

As a direct extension of the consensus statement of Fearon and coworkers, Martin and colleagues (2015), in a large cohort study of more than 8,000 patients with advanced cancer proposed that cachexia should be graded according to the concurrent Body Mass Index (BMI) and the degree of weight loss (WL) [6]. They showed that the BMI/WL grade had independent prognostic value and effectively stratified survival. More recently, this grading system has been reported to be associated with quality of life [7].

Therefore, while ECOG-PS, mGPS and BMI/WL grade are all associated with symptom burden and have valid prognostic value, to date, there has been no direct comparison of their prognostic value in patients with advanced cancer. Such a comparison may inform clinical practice as to which factors are associated with reduced survival and in turn inform the assessment and treatment of cancer cachexia. Therefore, the aim of the present study was to

81 compare the prognostic value of ECOG-PS, mGPS and BMI/WL in a prospective cohort of
82 patients with advanced cancer.

83

Patients and Methods

Patients:

An international database of patients with advanced cancer was analysed. All data were collected prospectively across 18 sites in the UK and Ireland (cancer centres, hospitals, and specialist palliative care units) over a five-year period (2011-2016). Eligible patients met the following criteria: ≥ 18 years of age; advanced cancer (defined as metastatic cancer [histological, cytological or radiological evidence], locally advanced or receiving anti-cancer therapy with palliative intent); able to complete study questionnaires; provide a venous blood sample and with a recorded ECOG-PS. Patients were excluded if they had breast or prostate carcinoma with only bone metastases as their survival times could be many years and therefore an argument could be made that they did not in fact have advanced cancer. Patients who were undergoing active anti-cancer therapy or not, on both an inpatient and outpatient basis were included. The study had ethics committee approval in both the UK and Ireland (UK-12/SS/0181 and Ireland EMC 4(g) 2015) and was conducted in accordance with the Declaration of Helsinki. All patients provided written informed consent. The study adhered to the STROBE guidelines for cohort studies.

Individual centres were opened at staggered time points. Within each centre, patients who fulfilled the eligibility criteria were invited to participate and consented on a sequential basis therefore reducing selection bias (Table 1). All assessments, including blood sampling, were performed on the day of consent.”

Prognostic markers

Clinicopathological data including the patient’s age, sex, ECOG-PS, mGPS, BMI/WL grade, underlying primary disease, and the presence of metastasis were recorded[2, 7, 8].

Bio-markers: C-reactive protein (CRP) and albumin combined in the mGPS. An autoanalyzer was used to measure serum CRP (mg/L) and albumin (g/L) concentrations (Architect; Abbot Diagnostics, Maidenhead, UK). The mGPS and BMI/WL grade was derived as previously described.[7, 9]

Statistical analysis:

Categorical variables were analysed using χ^2 test for linear-by-linear association, or χ^2 test for 2 by 2 tables. Patients were followed prospectively until the date of censoring (11/06/2018) or date of death from any cause (if present). Survival time was calculated from the date of recruitment to the date of death or censoring, whichever came first. Three month survival rate was examined since patients who have less than 3 month survival are considered to have refractory disease (cachexia) and allowed comparison with other studies [2, 5, 6]. Survival data were analysed using univariate and multivariate Cox regression. In addition to significant variables of interest on univariate analysis the predefined variables age, sex and cancer location were entered into a backward conditional multivariate model. Given the central prognostic role of performance status in patients with advanced cancer and the increased integration of oncology and palliative care ECOG-PS was taken as the primary stratification factor[10]. Cox Regression analysis was carried out for ECOG-PS, mGPS and BMI/WL grade to establish proportional Hazard Ratios.

Two tailed p values <0.05 were considered statistically significant. Statistical analysis was performed using SPSS software (Version 21.0. SPSS Inc., Chicago, IL, USA).

Results

A total of 730 patients (390 males, 340 females) met the eligibility criteria. The clinicopathological characteristics of the study population is shown in Table 2. The majority of patients were over 65 years of age (55.8%), had an ECOG-PS>0/1 (56.0%), mGPS>0 (55.5%), BMI/ weight loss grade 0/1 (55%) and had metastatic disease (85.8%). The majority of tumours were gastrointestinal (42.9%) and lung (28.2%) cancers. In those patients with tumours other than these the tumour types included Neurological 7 (1%), Urology 46 (6%), Gynaecological 33 (5%), Melanoma 28 (4%), Haematological 26 (4%), Breast 47 (6%), Unknown Primary 10 (1%), Others 14 (2%). The median overall survival (OS) for the entire cohort was 7.3 months (95% CI: 1.0-73.63 months). At the time of censoring, 182 patients (39.5%) were still alive. Median follow up time for these patients was 6.6 months (95% CI: 5.8-7.1 months).

The relationship between ECOG-PS, mGPS and BMI/WL grade and overall survival in patients with advanced cancer is shown in Table 3 and Figures 1-3. On multivariate cox regression analysis ECOG-PS (HR 1.61 95%CI 1.42-1.83, $p<0.001$), mGPS (HR 1.53, 95%CI 1.39-1.69, $p<0.001$) and BMI/WL grade (HR 1.41, 95%CI 1.25-1.60, $p<0.001$) remained independently associated with overall survival.

In patients with an ECOG-PS 0/1 the relationship between mGPS and BMI/WL grade and overall survival in patients with advanced cancer is shown in Table 3b. On multivariate cox regression analysis mGPS (HR 1.50, 95%CI 1.32-1.72, $p<0.001$) and BMI/WL Grade (HR 1.29, 95%CI 1.06-1.56, $p=0.009$) remained independently associated with overall survival.

In patients with an ECOG-PS 2 the relationship between mGPS and BMI/WL grade and overall survival in patients with advanced cancer is shown in Table 3c. On multivariate cox regression analysis mGPS (HR 1.56, 95%CI 1.32-1.86, $p<0.001$) and BMI/WL Grade (HR 1.46, 95%CI 1.19-1.80, $p<0.001$) remained independently associated with overall survival.

In patients with an ECOG-PS 3/4 the relationship between mGPS and BMI/WL grade and overall survival in patients with advanced cancer is shown in Table 3d. On multivariate cox regression analysis mGPS (HR 1.55, 95%CI 1.12-2.15, $p=0.009$) and BMI/WL grade (HR 1.53, 95%CI 1.11-2.12, $p=0.010$) remained independently associated with overall survival.

The relationship between ECOG-PS, mGPS and 3-month survival is shown in Table 4. In patients with an ECOG-PS of 0/1 there was a significant association between mGPS and 3-months survival ($p<0.001$). In patients with an ECOG-PS of 2 there was a significant association between mGPS and 3-months survival ($p<0.001$). In patients with an ECOG-PS of 3/4 there was a non-significant association between mGPS and 3-months survival ($p=0.102$). In patients with an ECOG-PS of 0-4 there was a significant association between mGPS and 3-months survival ($p<0.001$).

In patients with an mGPS of 0 there was a significant association between ECOG-PS and 3-months survival ($p<0.001$). In patients with an mGPS of 1 there was a significant association between ECOG-PS and 3-months survival ($p=0.021$). In patients with an mGPS of 2 there was a significant association between ECOG-PS and 3-months survival ($p<0.001$). In patients with an mGPS of 0-2 there was a significant association between ECOG-PS and 3-months survival ($p<0.001$).

The relationship between ECOG-PS, mGPS and 3-month survival in patients with a BMI/WL grade 0/1 is shown in Table 5. In patients with an ECOG-PS of 0/1 there was a significant association between mGPS and 3-months survival ($p=0.001$). In patients with an ECOG-PS of 2 there was a trend to a significant association between mGPS and 3-months survival ($p=0.085$). In patients with an ECOG-PS of 3/4 there was a non-significant association between mGPS and 3-months survival ($p=0.741$). In patients with an ECOG-PS of 0-4 there was a significant association between mGPS and 3-months survival ($p<0.001$).

In patients with an mGPS of 0 there was a significant association between ECOG-PS and 3-months survival ($p=0.001$). In patients with an mGPS of 1 there was a non-significant association between ECOG-PS and 3-months survival ($p=0.343$). In patients with an mGPS of 2 there was a significant association between ECOG-PS and 3-months survival ($p=0.003$). In patients with an mGPS of 0-2 there was a significant association between ECOG-PS and 3-months survival ($p<0.001$).

Discussion

The results of the present study show that, in a prospective cohort of patients with advanced cancer and a median survival of 7 months, the majority of patients had a good performance status, low BMI/WL grade (normal BMI, minimal weight loss) and had evidence of a systemic inflammatory response. Although ECOG-PS, mGPS and BMI/WL grade all effectively stratified overall survival when adjusted for age, sex and cancer location, both ECOG-PS and mGPS also stratified patient survival in those patients with a low BMI/WL grade. Therefore, the combination of ECOG-PS/ mGPS/ BMI/WL grade consistently stratifies survival in patients with advanced cancer [2, 5, 11].

The results of the present study are consistent with the work of Martin and colleagues who examined the relationship between weight loss grade, performance status and the GPS in more than 2,500 patients with advanced cancer and a median survival of 7.6 months [12]. Unfortunately, to date this data has only been published in abstract form. Nevertheless, the tabulated data presented in abstract are consistent with the present analysis and their conclusions that “a combination of BMI/ WL grades, PS and GPS consistently stratifies advanced cancer patients into very different survival groups, and could be considered as diagnostic criteria for cachexia” have been confirmed and extended in the present study [12]. For example, in the present study, in Table 5, the numbers of patients with ECOG-PS 3-4 cohort (BMI/WL grade 0/1) were relatively small (n=33) and the mGPS did not significantly stratify survival. However, in the study of Martin and colleagues [11] in a larger cohort (n=2,656) the numbers of patients with ECOG-PS 3-4 was 96 and mGPS significantly stratified survival. Therefore, the ECOG-PS 3-4 subsample in the present study was likely to be underpowered. It remains to be whether BMI/WL grade as an indicator of nutritional risk is superior to routine clinical screening tools such as MUST [13]. Moreover, such work is the

basis of the rationalisation of the multiple tools developed to identify clinically important cachexia, sarcopenia and malnutrition.

The results of the present study indicate the importance of the systemic inflammatory response not only as a prognostic factor but also to inform the nutritional and functional decline associated with advanced cancer. Indeed, in those patients who had both a good performance status and good BMI/WL grade (no obvious functional decline or weight loss), the mGPS effectively stratified median survival between 11.4 months and 7.5 months. Furthermore, in those patients, 42% had an elevated mGPS. One interpretation of the findings is that obvious weight loss in patients with advanced cancer is a later event than functional decline, and that functional decline is a later event than the development of a systemic inflammatory response [14]. Therefore, it may be that the mGPS should form the basis of stratification of likely survival in patients with advanced cancer. Indeed, the prognostic value of the mGPS has been extensively validated in early stage disease [15]. Moreover, some workers have proposed that in “the more aggressive tumour types (e.g. pancreas and lung), the future of patients with elevated mGPS scores is so grim that they should be given precachexia status and offered multimodal therapy which may delay the onset of cachexia and/or death [16]. Also, Morley (2019) commented that although the cachexia score (CASCO) has been identified “as the best screening test available for cachexia, a quicker screen that may be equally effective is the Glasgow Prognostic Score” [17]. Irrespective, greater prominence should be given to the assessment of the systemic inflammatory response (as evidenced by the mGPS) in patients with advanced cancer [3]. Moreover, the systemic inflammatory response may be considered a cardinal feature of the syndrome of cancer cachexia [18, 19]. If this proves to be the case then the systemic inflammatory response will become an important therapeutic target for cancer cachexia in the coming years [20]. Indeed, targeting the inflammatory response to treat cancer cachexia has

been proposed as a therapy with clinical trials now underway [21, 22]. Trials have examined this in the past but importantly patients were not entered into these trials on the basis of their systemic inflammatory response.

The present study had a number of limitations. The majority of patients were undergoing palliative care. As a result, it could be assumed that there had a high symptom burden which has been shown to be associated with worse outcomes. Furthermore, despite recruitment occurring across 18 sites, the patient cohort may not be completely representative of patients with advanced cancer. However, they were well defined in terms of the components of known and validated prognostic scores which will allow for direct comparison with other populations in future studies. Finally, the method of patient recruitment/sampling strategy was opportunistic. However, the heterogeneity of the primary cancer types suggests that the recruitment process while being opportunistic was robust.

In summary, while ECOG-PS, mGPS and BMI/WL grade are all valid prognostic scores and may form the basis of future risk stratification of survival in patients with advanced cancer.

Acknowledgments:

The contribution of the authors is outlined below and there are no conflicts of interest to report for any of the authors.

- Ross D Dolan: Data interpretation and writing of the manuscript
- Louise Daly: Data interpretation and writing of the manuscript
- Wei MJ Sim: Assistant in writing of the manuscript
- Marie Fallon: Supervision and assistance with the manuscript
- Aoife Ryan: Supervision and assistance with the manuscript

- 259 • Donald C McMillan: Senior author who assisted with the manuscript and data
- 260 interpretation
- 261 • Barry J Laird: Senior author who assisted with the manuscript and data
- 262 interpretation

References:

- [1] Wallengren O, Iresjö BM, Lundholm K, Bosaeus I. Loss of muscle mass in the end of life in patients with advanced cancer. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*. 2015;23:79-86.
- [2] Laird BJ, Fallon M, Hjermstad MJ, Tuck S, Kaasa S, Klepstad P, et al. Quality of Life in Patients With Advanced Cancer: Differential Association With Performance Status and Systemic Inflammatory Response. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2016;34:2769-75.
- [3] Dolan RD, McSorley ST, Horgan PG, Laird B, McMillan DC. The role of the systemic inflammatory response in predicting outcomes in patients with advanced inoperable cancer: Systematic review and meta-analysis. *Crit Rev Oncol Hematol*. 2017;116:134-46.
- [4] Simmons C, McMillan DC, Tuck S, Graham C, McKeown A, Bennett M, et al. "How Long Have I Got?"-A Prospective Cohort Study Comparing Validated Prognostic Factors for Use in Patients with Advanced Cancer. *The oncologist*. 2019.
- [5] Laird BJ, Kaasa S, McMillan DC, Fallon MT, Hjermstad MJ, Fayers P, et al. Prognostic factors in patients with advanced cancer: a comparison of clinicopathological factors and the development of an inflammation-based prognostic system. *Clinical cancer research : an official journal of the American Association for Cancer Research*. 2013;19:5456-64.
- [6] Martin L. Diagnostic criteria for cancer cachexia: data versus dogma. *Current opinion in clinical nutrition and metabolic care*. 2016;19:188-98.
- [7] Martin L, Senesse P, Gioulbasanis I, Antoun S, Bozzetti F, Deans C, et al. Diagnostic criteria for the classification of cancer-associated weight loss. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2015;33:90-9.

- [8] Park JH, Ishizuka M, McSorley ST, Kubota K, Roxburgh CSD, Nagata H, et al. Staging the tumor and staging the host: A two centre, two country comparison of systemic inflammatory responses of patients undergoing resection of primary operable colorectal cancer. *American journal of surgery*. 2017.
- [9] McMillan DC. Cancer and systemic inflammation: stage the tumour and stage the host. *Br J Cancer*. 2013;109:529.
- [10] Kaasa S, Loge JH, Aapro M, Albrecht T, Anderson R, Bruera E, et al. Integration of oncology and palliative care: a Lancet Oncology Commission. *Lancet Oncol*. 2018;19:e588-e653.
- [11] Laird BJ, Scott AC, Colvin LA, McKeon AL, Murray GD, Fearon KC, et al. Cancer pain and its relationship to systemic inflammation: an exploratory study. *Pain*. 2011;152:460-3.
- [12] Martin L, Senesse P, Gioulbasanis I, Lundholm K, Bosaeus I, Voss AC, et al. The combination of weight loss grade, performance status, and Glasgow Prognostic Score contribute to survival discrimination in advanced cancer patients at risk for cachexia. 8th Cachexia Conference Paris *Journal of Cachexia, Sarcopenia and Muscle*; 2015. p. 446.
- [13] Arends J, Baracos V, Bertz H, Bozzetti F, Calder PC, Deutz NEP, et al. ESPEN expert group recommendations for action against cancer-related malnutrition. *Clinical nutrition* (Edinburgh, Scotland). 2017;36:1187-96.
- [14] Dolan RD, Daly LE, Simmons C, Ryan A, Sim WS, Fallon M, et al. The relationship between ECOG-PS/mGPS (modified Glasgow prognostic score) framework, CT-derived body composition, physical function tests and survival in patients with advanced cancer. *JAMA Oncology* 2018;In Press.
- [15] Dolan RD, Lim J, McSorley ST, Horgan PG, McMillan DC. The role of the systemic inflammatory response in predicting outcomes in patients with operable cancer: Systematic review and meta-analysis. *Sci Rep*. 2017;7:16717.

- [16] MacDonald N. Terminology in cancer cachexia: importance and status. *Current opinion in clinical nutrition and metabolic care*. 2012;15:220-5.
- [17] Morley JE. Editorial: Screening for Malnutrition (Undernutrition) in Primary Care. *J Nutr Health Aging*. 2019;23:1-3.
- [18] Douglas E, McMillan DC. Towards a simple objective framework for the investigation and treatment of cancer cachexia: the Glasgow Prognostic Score. *Cancer treatment reviews*. 2014;40:685-91.
- [19] Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, et al. ESPEN guidelines on nutrition in cancer patients. *Clinical nutrition (Edinburgh, Scotland)*. 2017;36:11-48.
- [20] Diakos CI, Charles KA, McMillan DC, Clarke SJ. Cancer-related inflammation and treatment effectiveness. *Lancet Oncol*. 2014;15:e493-503.
- [21] Solheim TS, Laird BJA, Balstad TR, Bye A, Stene G, Baracos V, et al. Cancer cachexia: rationale for the MENAC (Multimodal-Exercise, Nutrition and Anti-inflammatory medication for Cachexia) trial. *BMJ Support Palliat Care*. 2018.
- [22] McDonald JJ, McMillan DC, Laird BJ. Targeting IL-1alpha in cancer cachexia: a narrative review. *Curr Opin Support Palliat Care*. 2018.

Table 1. Summary table of recruitment centres including patient numbers

Centres	Overall numbers Recruited	Numbers Excluded	Numbers included in Final Analysis
Abersy	31 (3.0)	2 (0.7)	29 (4.0)
Beatson Glasgow	96 (9.3)	1 (0.3)	95 (13.0)
Coventry	29 (2.8)	3 (1.0)	26 (3.6)
CUH	166 (16.2)	155 (52.2)	11 (1.5)
Denbigh	54 (5.3)	13 (4.4)	41 (5.6)
Eastwood	26 (2.5)	3 (1.0)	23 (23.2)
Edinburgh	15 (1.5)	3 (1.0)	12 (1.6)
Gwyned	22 (2.1)	0 (0.0)	22 (3.0)
Hayward	34 (3.3)	2 (0.7)	32 (4.4)
MUH	383 (37.3)	59 (19.9)	324 (44.4)
Nighting	27 (2.6)	6 (2.0)	21 (2.9)
Port Talbert	2 (0.2)	1 (0.3)	1 (0.1)
PPWH	17 (1.7)	2 (0.7)	15 (2.1)
Scar	4 (0.4)	3 (1.0)	1 (0.1)
St. Andrews	9 (0.9)	1 (0.3)	8 (1.1)
St Gem	70 (6.8)	33 (11.1)	37 (5.1)
Strathclyde	5 (0.5)	1 (0.3)	4 (0.5)
Wrexham	37 (3.6)	9 (3.0)	28 (3.8)
Total	1027	297	730

Table 2. Clinicopathological characteristics of patients with advanced cancer (n=730)

Characteristic		
		n=730 (%)
	Clinico-pathological	
Age	<65	323 (44.2)
	65 - 74	225 (30.8)
	>74	182 (24.9)
Sex	Male	390 (53.4)
	Female	340 (46.6)
Cancer Location	Lung	206 (28.2)
	GI	313 (42.9)
	Other	211 (28.9)
Metastatic Disease	No	104 (14.2)
	Yes	626 (85.8)
	Previous Ant-Cancer Therapy	
Chemotherapy	No	148 (20.3)
	Yes	582 (79.7)
Radiotherapy	No	572 (78.4)
	Yes	158 (21.6)
Hormones	No	678 (92.9)
	Yes	52 (7.1)
	Performance status	
ECOG-PS¹	0/1	409 (56.0)
	2	240 (32.9)
	3/4	81 (11.1)
	Systemic Inflammation	
mGPS¹	0	325 (44.5)
	1	111 (15.2)
	2	294 (40.3)
	Body composition	
BMI[‡]	≤20.0 kg/m ²	99 (13.6)
	20-21.9 kg/m ²	92 (12.6)
	22-24.9 kg/m ²	174 (23.4)
	25-27.9 kg/m ²	156 (21.4)
	≥28.0 kg/m ²	209 (28.6)
% Weight Loss	<2.5	415 (56.8)
	≥2.5	315 (43.2)
BMI/WL grade[‡]	0/1	404 (55.3)
	2/3	241 (33.0)
	4	85 (11.6)

¹ ECOG-P: Eastern Cooperative Oncology Group Performance Status, ¹ mGPS: modified Glasgow Prognostic Score, [‡] BMI: [‡]Body Mass

Index, BMI/WL grade: Body Mass Index/Weight Loss Grade

Table 3. The relationship between ECOG, mGPS and BMI/WL grade and overall survival in patients with advanced cancer.

Characteristics	Univariate	p-value	Multivariate	p-value	Multivariate Adjusted for Age, Sex and Cancer Location	p-value
Table 3a ECOG-PS 0/1-4 (n=730)						
ECOG-PS [†]	1.85 (1.63-2.09)	<0.001	1.61 (1.42-1.83)	<0.001	1.64 (1.44-1.86)	<0.001
mGPS [†]	1.63 (1.48-1.80)	<0.001	1.53 (1.39-1.69)	<0.001	1.49 (1.35-1.64)	<0.001
BMI/WL grade [‡]	1.48 (1.30-1.67)	<0.001	1.41 (1.25-1.60)	<0.001	1.39 (1.23-1.58)	<0.001
Table 3b ECOG-PS 0/1 (n=409)						
mGPS [†]	1.51 (1.32-1.72)	<0.001	1.50 (1.32-1.72)	<0.001	1.44 (1.26-1.65)	<0.001
BMI/WL grade [‡]	1.29 (1.07-1.56)	0.007	1.29 (1.06-1.56)	0.009	1.25 (1.03-1.51)	0.024
Table 3b ECOG-PS 2 (n=240)						
mGPS [†]	1.59 (1.34-1.89)	<0.001	1.56 (1.32-1.86)	<0.001	1.53 (1.28-1.82)	<0.001
BMI/WL grade [‡]	1.50 (1.22-1.84)	<0.001	1.46 (1.19-1.80)	<0.001	1.43 (1.16-1.76)	0.001
Table 3c ECOG-PS 3-4 (n=81)						
mGPS [†]	1.42 (1.04-1.95)	0.029	1.55 (1.12-2.15)	0.009	1.54 (1.11-2.14)	0.009
BMI/WL grade [‡]	1.37 (1.02-1.84)	0.039	1.53 (1.11-2.12)	0.010	1.58 (1.15-2.19)	0.005

[†] ECOG-P: Eastern Cooperative Oncology Group Performance Status, [†] mGPS: modified Glasgow Prognostic Score, [‡] BMI: [‡]Body Mass Index, BMI/WL grade: Body Mass Index/Weight Loss Grade. Statistical analysis was with univariate and multivariate Cox regression analysis.

Table 4. The relationship between the ECOG-PS, mGPS and 3 month survival rate in patients with advanced cancer (n=730)

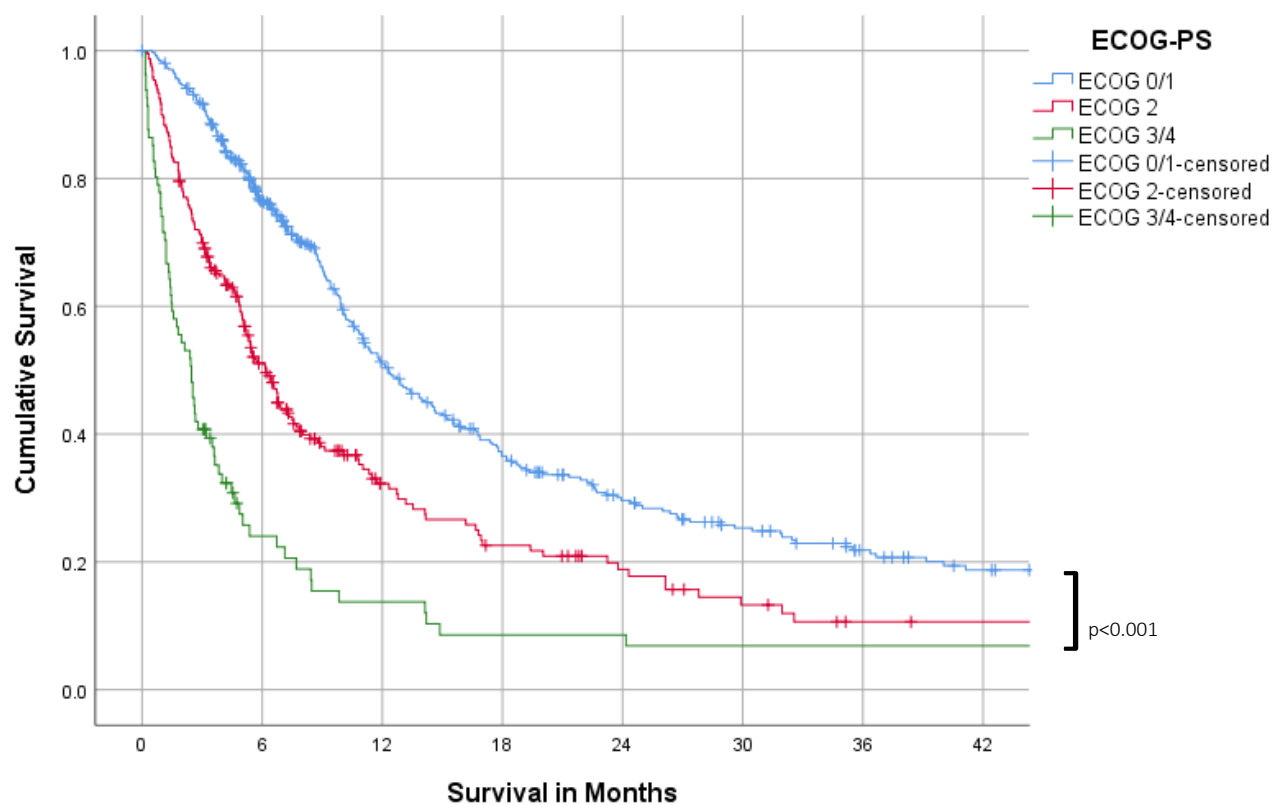
ECOG-PS ¹		mGPS ¹ =0	mGPS ¹ =1	mGPS ¹ =2	mGPS ¹ 0-2	
		n (%)	n (%)	n (%)	n (%)	P-value
0-1	n	226	56	127	409	
	Survival Rate at 3 months	218 (96.5%)	46 (82.1%)	105 (82.7%)	369 (90.26%)	<0.001
	Median Survival	10.9	7.0	7.0	9.1	
	95% CI	9.2-12.3	5.3-10.2	5.7-8.9	8.0-10.0	
2	n	87	42	111	240	
	Survival Rate at 3 months	76 (87.4%)	28 (66.7%)	62 (55.9%)	166 (69.2%)	<0.001
	Median Survival	7.3	5.0	3.5	5.2	
	95% CI	6.1-9.8	3.1-6.6	2.6-4.8	4.6-5.7	
3-4	n	12	13	56	81	
	Survival Rate at 3 months	8 (66.7%)	6 (46.2%)	19 (33.9%)	33 (40.7%)	0.102
	Median Survival	5.9	2.6	1.9	2.5	
	95% CI	2.5-14.2	0.6-4.5	1.2-2.7	1.5-3.1	
ECOG-PS¹ 0/1-4	n	325	111	294	730	
	Survival Rate at 3 months	302 (92.9%)	80 (72.1%)	186 (63.3%)	568 (77.8%)	<0.001
	Median Survival	9.6	5.3	4.2	6.6	
	95% CI	8.4-10.8	4.2-6.6	3.6-5.1	5.8-7.1	
P-value		<0.001	0.021	<0.001	<0.001	

¹ ECOG-P: Eastern Cooperative Oncology Group Performance Status, ¹ mGPS: modified Glasgow Prognostic Score. Statistical analysis was with χ^2 test for linear-by-linear association, or χ^2 test for 2 by 2 tables.

Table 5. The relationship between the ECOG-PS, mGPS and 3 month survival rate in patients with a BMI/WL grade 0/1 and advanced cancer (n=404)

ECOG-PS ¹		mGPS ¹ =0	mGPS ¹ =1	mGPS ¹ =2	mGPS ¹ 0-2	
		n (%)	n (%)	n (%)	n (%)	P-value
0-1	n	148	32	73	253	
	Survival Rate at 3 months	144 (97.3%)	26 (81.3%)	62 (84.9%)	232 (91.7%)	0.001
	Median Survival	11.4	9.4	7.5	9.9	
	95% CI	9.2-14.4	4.0-17.8	6.1-9.9	8.7-11.4	
2	n	49	24	45	118	
	Survival Rate at 3 months	44 (89.8%)	21 (87.5%)	33 (73.3%)	98 (83.1%)	0.085
	Median Survival	7.9	6.6	4.9	6.7	
	95% CI	6.8-10.7	5.0-8.9	3.7-6.6	5.2-7.6	
3-4	n	6	5	22	33	
	Survival Rate at 3 months	4 (66.7%)	3 (60%)	11 (50.0%)	18 (54.5%)	0.741
	Median Survival	7.2	3.4	2.9	3.2	
	95% CI	1.0-73.2	0.6-8.4	1.2-5.0	1.8-5.0	
ECOG-PS¹ 0/1-4	n	203	61	140	404	
	Survival Rate at 3 months	192 (94.6%)	50 (82.0%)	106 (75.7%)	348 (86.1%)	<0.001
	Median Survival	10.0	7.5	5.7	7.9	
	95% CI	8.9-11.7	5.8-8.9	4.8-7.1	7.3-8.9	
P-value		0.001	0.343	0.003	<0.001	

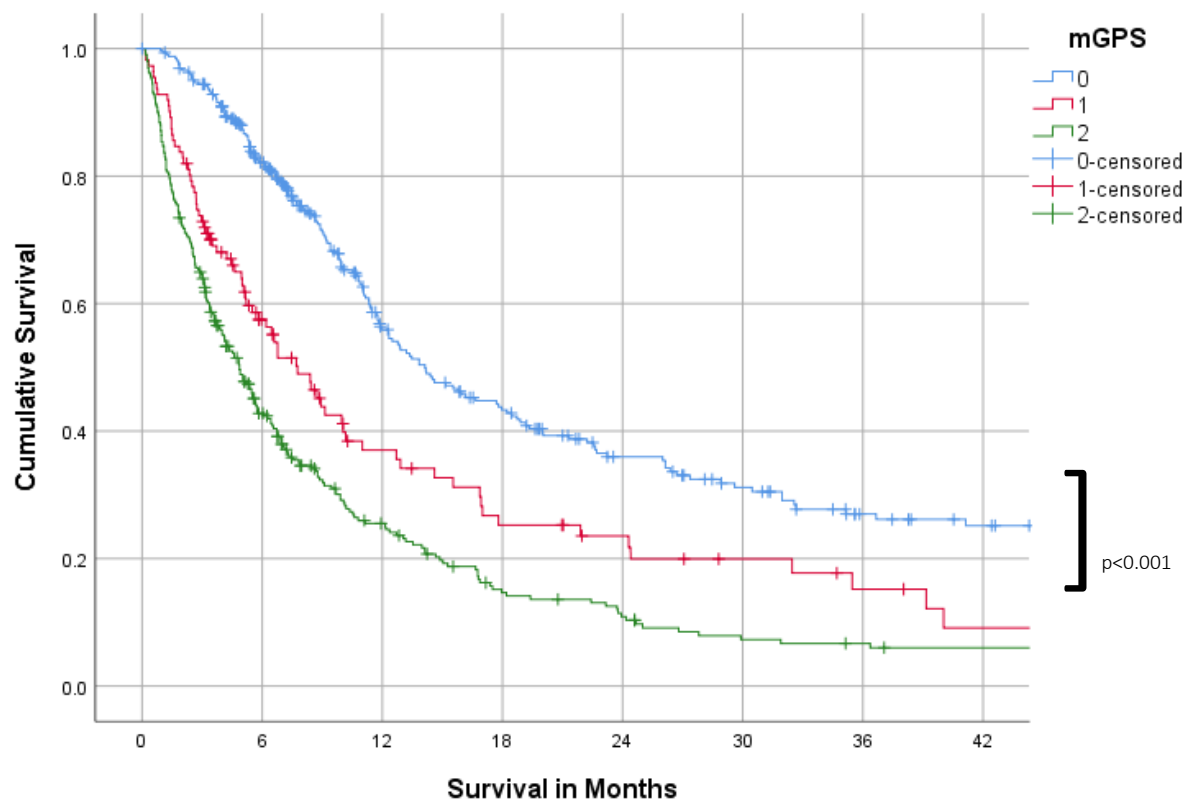
¹ ECOG-P: Eastern Cooperative Oncology Group Performance Status, ¹ mGPS: modified Glasgow Prognostic Score. Statistical analysis was with χ^2 test for linear-by-linear association, or χ^2 test for 2 by 2 tables.



	0 months	6 months	12 months	18 months	24 months	30 months	36 months	42 months
ECOG 0/1	409	317	236	194	176	166	159	154
ECOG 2	240	127	95	83	79	74	72	72
ECOG 3/4	81	22	16	13	12	12	12	12

Figure 1.0: The relationship between the ECOG-PS and OS in patients with advanced cancer (n=730, Log rank

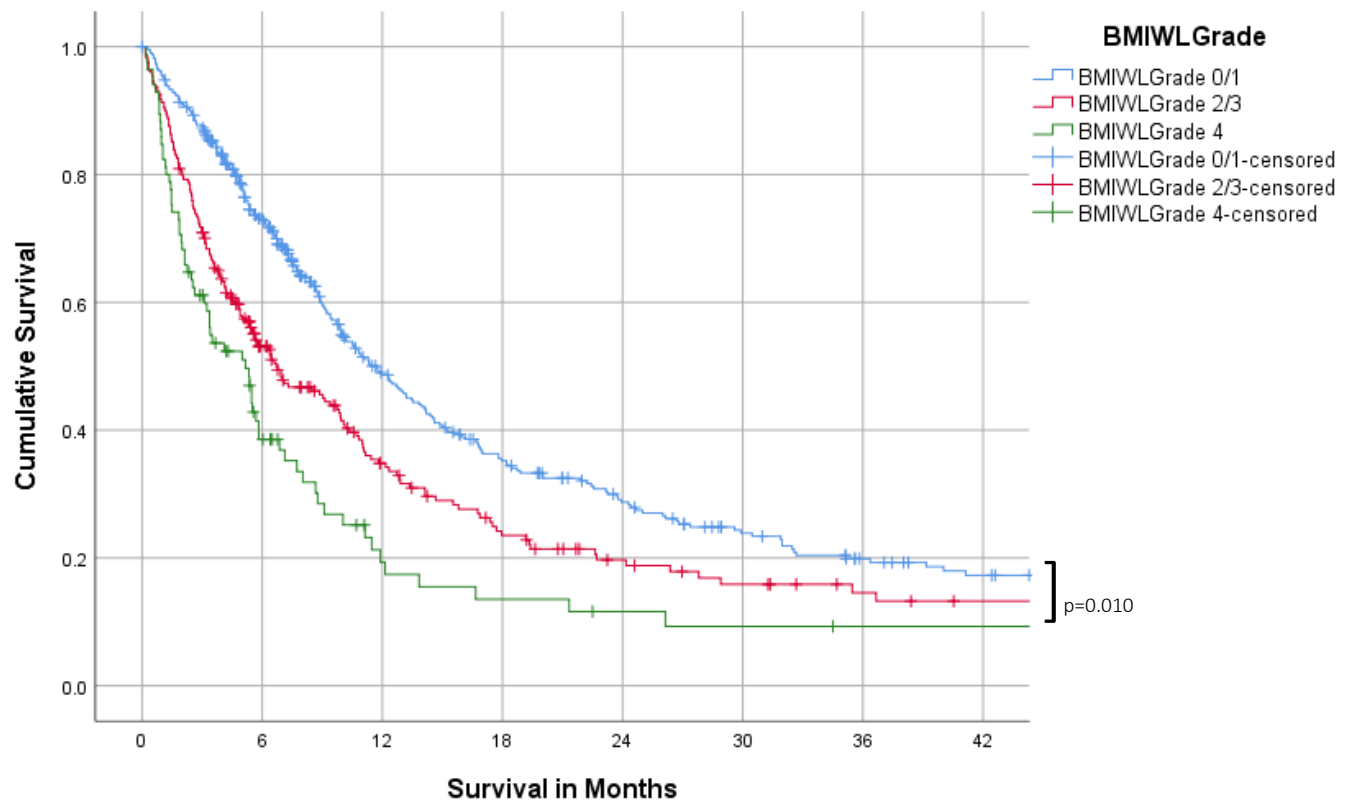
test: ECOG-PS 0/1-2: $p < 0.001$, ECOG-PS 2-3/4: $p < 0.001$, ECOG-PS 0/1-3/4: $p < 0.001$)



	0 months	6 months	12 months	18 months	24 months	30 months	36 months	42 months
mGPS 0	325	270	207	180	166	158	152	150
mGPS 1	111	66	50	42	41	39	37	35
mGPS 2	294	130	90	68	61	55	64	53

Figure 2.0: The relationship between the mGPS and OS in patients with advanced cancer (n=730, Log rank test:

mGPS 0-1: $p < 0.001$, mGPS1-2: 0.006, mGPS 0-2: $p < 0.001$)



	0 months	6 months	12 months	18 months	24 months	30 months	36 months	42 months
BMIWLGrade 0/1	404	300	224	187	171	160	152	148
BMIWLGrade 2/3	241	131	99	82	77	73	72	71
BMIWLGrade 4	85	35	24	21	20	19	19	19

Figure 3.0: The relationship between the BMIWL grade and OS in patients with advanced cancer (n=730, Log rank test: BMIWL grade 0/1-2/3: $p<0.001$, BMIWL grade 2/3-4: $p<0.001$, ECOG-PS 0/1-4: $p=0.010$)